Type IV thoracoabdominal aortic aneurysm with lymphoplasmacytic aortitis and cystic medial degeneration in a 32-year-old patient with Marfan syndrome

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Aortitis identified in approximately 12% of all thoracoabdominal aneurysms. The most common subtype of inflammatory aortitis is giant cell aortitis, followed by lymphoplasmacytic aortitis. Inflammatory aortitis may occur in isolation or as part of a systemic inflammatory disorder such as Takayasu arteritis, systemic lupus erythematosus, rheumatoid arthritis, and giant cell arteritis. Aortitis has not been described in patients with Marfan syndrome. We report the case of a 32-year-old man with Marfan syndrome and a strong family history of aneurysmal disease who presented with an asymptomatic Crawford type IV thoracoabdominal aneurysm. His aneurysm had no associated dissection, and surgical pathology revealed severe medial degeneration and lymphoplasmacytic aortitis. To our knowledge, this is the first report of such a finding in a patient with Marfan syndrome. (J Vasc Surg 2005;42:168-71.)

Thoracic aortic aneurysms, dissections, and aortic rupture are common cardiovascular manifestations of Marfan syndrome (MFS).[1] When compared with patients with degenerative thoracoabdominal aneurysms (TAAs), patients with MFS have a higher incidence (50% vs 27.7%) of more extensive aneurysms (Crawford type II),[2] which involve all or most of the descending thoracic and abdominal aorta. Patients with MFS also have a higher incidence of associated aortic dissections. (82% vs 21%).[1] Aneurysms that involve all or most of the abdominal aorta (Crawford type IV) constitute approximately 18% of TAAs in patients with MFS.[1] Most of these aneurysms in patients with MFS have a disruption of medial and adventitial elastin and collagen in association with necrosis of the medial smooth muscle cells and accumulation of proteoglycans, a histologic lesion termed cystic medial degeneration (CMD).[3,4] This noninflammatory lesion is associated with abnormal fibrillin 1 synthesis due to a mutation in the *FBN1* gene on chromosome 15 in patients with MFS.[3] An inflammatory infiltrate of the aortic wall (aortitis) in aortic aneurysms is uncommon. A recent 20-year review of pathologic specimens from consecutive aortic surgeries revealed that only 52 of 1204 specimens (4.3%) were classified as idiopathic aortitis, a designation that required exclusion of vasculitis associated with postoperative infections, atherosclerosis, or inflammation occurring around surgical materials from previous operations. If one considered only thoracic aortic aneurysms, 12% of 386 thoracic specimens had idiopathic inflammatory features.[5] Noninfectious aortitis may occur in isolation or as part of a systemic inflammatory disorder such as Takayasu arteritis, systemic lupus erythematosus, rheumatoid arthritis, and giant cell arteritis.[6-9] Aortitis has not yet been reported in patients with MFS.

We report the case of a 32-year-old man with MFS and a strong family history of aneurysmal disease who presented with an asymptomatic aneurysm that involved the abdominal aorta from the level of the diaphragm to the aortic bifurcation (Crawford type IV).[2] This aneurysm had no associated dissection. Surgical pathology revealed severe medial degeneration characterized by elastic tissue loss and lymphoplasmacytic aortitis. To our knowledge, this is the first report of such a finding in a patient with MFS.

CASE REPORT

The patient presented is a 32-year-old man who was diagnosed with MFS at age 3. He had a strong family history of both ascending and descending aortic aneurysms. He had been carefully followed since childhood and 16 months before presentation, an ultrasound scan of the abdomen identified a 4-cm abdominal aortic aneurysm. Four months later, a computed tomography (CT) scan of the abdomen revealed a fusiform infrarenal aneurysm measuring 5.2 cm. At the time of the presentation, a CT scan confirmed a 5.9-cm aneurysm that extended from the level of the diaphragm to the aortic bifurcation, consistent with a Crawford type IV thoracoabdominal aortic aneurysm. His medical history was significant for multiple sclerosis, depression, and bilaterally displaced lenses, and he met the diagnostic criteria for MFS. His surgical history was significant only for a tonsillectomy. His father and two paternal aunts had undergone open surgical repair of aortic aneurysms before age 55 (ascending and abdominal, ascending, and thoracoabdominal, respectively). One of these aunts and her two children had been diagnosed with MFS. On physical examination, he had the typical features of MFS. His height was 6 ft 5 in. A prominent

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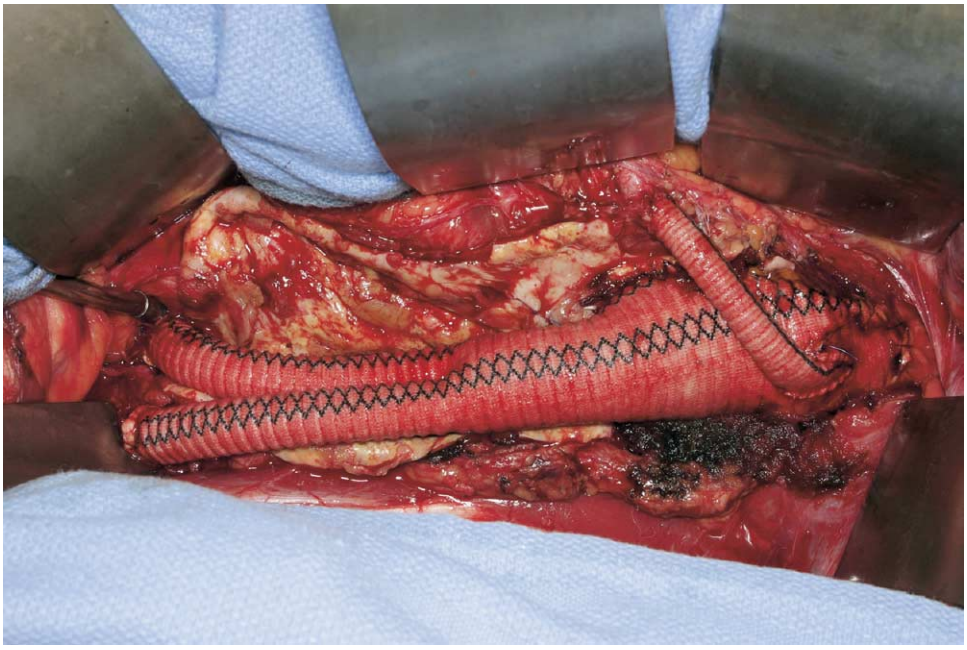

Fig 1. Intraoperative image illustrates the bifurcated, gelatin-coated polyester graft from the level of the diaphragm to both mid common iliac arteries.

aneurysmal aortic pulse was noted in the upper abdomen. His upper and lower extremity pulses were all normal. Laboratory studies were remarkable only for a white blood cell count of 5.5×10^9/L (normal range, $3.5-10.5 \times 10^9$/L) with 0.71×10^9/L lymphocytes (normal range, $0.9-2.9 \times 10^9$/L). Because there was no reason to suspect a vasculitic disorder, autoimmune serologic studies and markers of inflammation were not obtained. His preoperative evaluation included a transthoracic echocardiogram that showed findings consistent with MFS. These consisted of mild ascending aortic dilatation (37 mm) and mitral valve prolapse with a mildly thickened mitral valve with trivial regurgitation. The aortic valve and left ventricle were normal. A CT scan of the chest and abdomen identified a thoracoabdominal aortic aneurysm with a diameter of 59 mm.

His type IV thoracoabdominal aortic aneurysm was repaired with the insertion of a 22 × 11-mm bifurcated, gelatin-coated polyester graft from the level of the diaphragm to both mid common iliac arteries. Two pairs of intercostal arteries, the celiac and the superior mesenteric arteries, and the right renal artery were incorporated with an aortic cuff into the proximal anastomosis. The left renal artery was revascularized using a 7-mm interposition gelatin-coated polyester graft (Fig 1). Cerebrospinal fluid drainage was used during the procedure. The patient tolerated the procedure well, and his postoperative recovery was uneventful. He was dismissed on the sixth postoperative day. Surgical pathology revealed lymphoplasmacytic aortitis and medial degeneration composed mainly of diffuse and severe loss of elastic fibers without pooling of proteoglycans (Figs 2 and 3). Six months after the procedure, the patient is completely asymptomatic and has resumed his normal activities.

DISCUSSION

Approximately 6.3% of all TAAs requiring surgical intervention are associated with MFS.[1] Half of these aneurysms (50%) involve the descending thoracic and most of the abdominal (Crawford type II), and the majority (>80%) are associated with an aortic dissection.[1] CMD is the usual histologic finding in aortic aneurysms in patients with MFS and is also noted commonly in thoracic aneurysms in patients without MFS.[4]

The patient presented stands out in that he had a type IV aneurysm, with no associated dissection and lymphoplasmacytic aortitis, which has not yet been reported in MFS.

The simultaneous occurrence of these findings could be simply coincidental; however, we believe that the identified aortitis suggests that an autoimmune process may play a role in this somewhat atypical aneurysm in a patient who carries the diagnosis of multiple sclerosis, which itself is considered an autoimmune disease characterized by immune-initiated inflammatory demyelination of nerve fibers.

The typical histologic lesion in the aortic tissue of patients with MFS, CMD is characterized mainly by the degeneration of elastic fibers in the medial layer of the aorta with variable accumulation of pools of glycosaminoglycans. CMD is not a specific finding of MFS and can be seen in other heritable disorders of connective tissue, such as the Ehlers-Danlos syndrome.[10] It is also seen in patients without inherited connective tissue disease and may be associated with certain risk factors such as systemic hypertension and bicuspid aortic valve. In patients with inherited con-

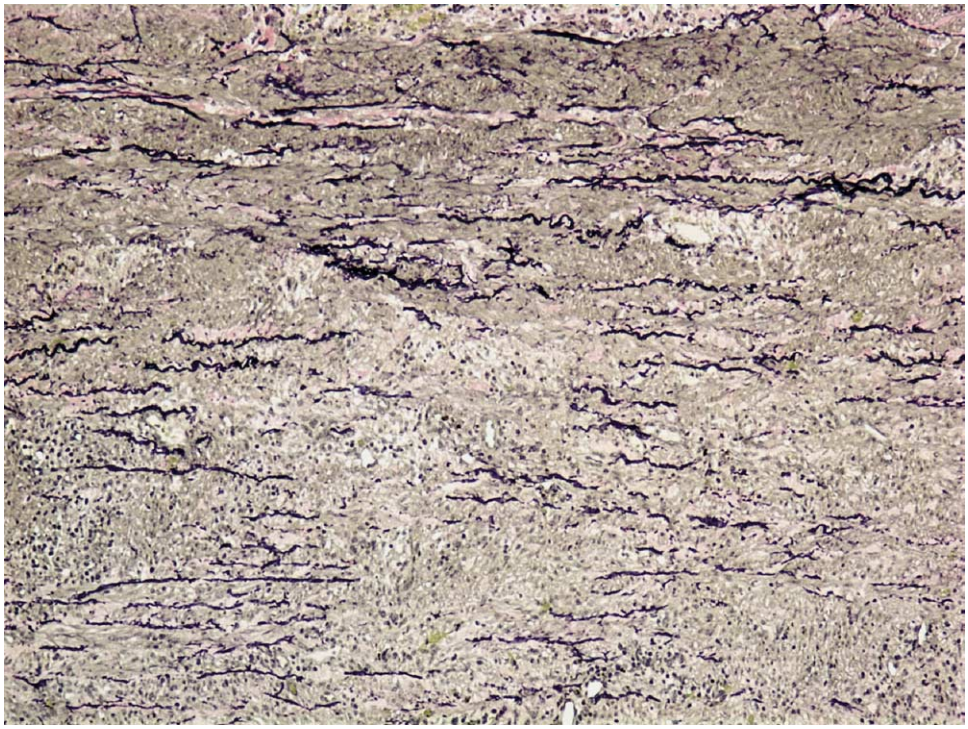

Fig 2. Intermediate power photomicrograph illustrates the diffuse loss of the medial elastic fibers, not limited to areas of medial inflammation (Verhoeff–van Gieson stain, ×100).

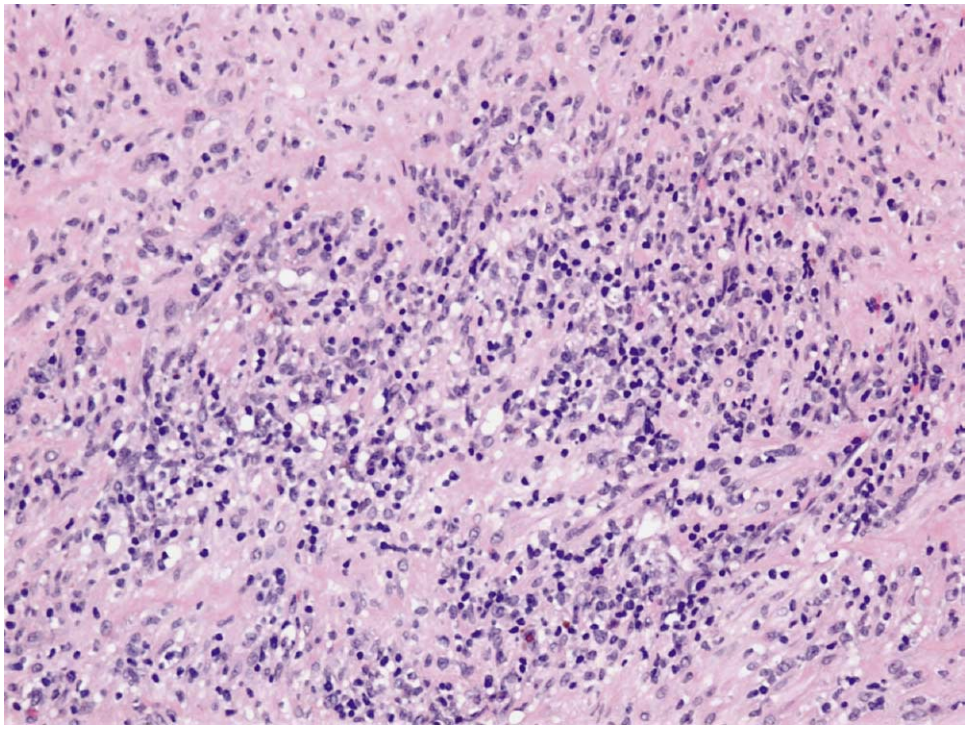

Fig 3. Multiple scattered foci of medial inflammation composed mainly of lymphocytes, plasma cells, and histiocytes without multinucleated giant cells are also identified, defining lymphoplasmacytic aortitis (hematoxylin and eosin, ×200).

nective tissue disease, CMD occurs at a younger age and is usually greater in extent and severity.[10]

Aortitis is less common than CMD and is seen in approximately 16% of all ascending and TAAs that require surgical intervention.[4,5] The most common subtype of aortitis is giant cell aortitis.[10] Lymphoplasmacytic aortitis is much less common and is characterized by medial inflammation composed of lymphocytes and plasma cells without giant cells or granulomas.[8] Patients with aortitis have a significantly higher incidence of autoimmune disease when compared with controls (19% vs 0%).[5] Aortitis may occur in isolation or as part of a systemic inflammatory disorder such as Takayasu arteritis, systemic lupus erythematosus, rheumatoid arthritis, and giant cell arteritis.[5-9] Aortitis has not been described in MFS. Although the patient presented here had multiple sclerosis, which is often considered an autoimmune process, aortitis has not been associated with it.

In our patient, CMD was mostly characterized by fragmentation and loss of elastic fibers without significant accumulation of glycosaminoglycans. The loss of elastic tissue was not limited to the areas of medial inflammation and extended to other areas of the specimen, indicating that this process was not localized and involved the entire aorta and implying a more systemic process.

Treatment of aneurysms with associated aortitis is not different from that of other aneurysms. Although patients with MFS occasionally require more extensive operations, several studies have shown that aortic reconstruction for both patients with Marfan-related aneurysms and patients with aortitis can be performed safely. Indications, treatment, and prognosis of both patient groups are the same when compared with those of other patients with aortic aneurysms.[11,12]

The role of medical treatment of aortitis-related aneurysms with immunosuppressive therapy remains uncertain. In a recent retrospective study, 36 patients with follow-up of more than 42 months after aortic surgery, new aneurysms were identified in 6 of 25 patients who were not treated with glucocorticosteroids and in none of 11 patients who were treated with glucocorticosteroids.[5] Although the observations could indicate a benefit of such therapy in this setting, marked variation of dose and duration of therapy raises uncertainty about the efficacy of therapy and such therapy may outweigh the hypothetical benefit of preventing progression or recurrence of the inflammatory process. Because 17% of patients subsequently developed new aneurysms, patients with aortitis-associated aneurysms should be periodically evaluated for recurrent disease and immunosuppressive treatment should be considered on an individual basis.

Patients with MFS often require new surgical interventions after undergoing aortic operations. In a study designed to determine long-term results of aortic surgery, 101 of 192 (52.6%) patients required a second operation to repair aneurysms that developed at a different site.[13]

In our patient, the strong family history of aneurysmal disease and the development of thoracoabdominal aneurysm in three close relatives suggest a genetic component to his aneurysm formation. Because patients with aortitis and patients with MFS have a higher risk of recurrence, the risk of recurrence in this particular patient and his family may be much higher than of other patients with MFS. We are planning to follow this patient and his family very closely for the development of new aneurysms and will attempt to determine whether other aneurysms also have evidence of aortitis.

CONCLUSIONS

This case represents the first reported case of lymphoplasmacytic aortitis in a patient with MFS. It illustrates a young patient with an uncommon problem in which surgical treatment resulted in a good outcome. The coincidence of aortitis and MFS may place this patient at higher risk of aneurysm recurrence when compared when other patients with MFS. Further genetic and biochemical studies may lead to better understanding of the pathogenesis of aortic aneurysm in similar patients.

REFERENCES

1. Coselli JS, LeMaire SA. Current status of thoracoabdominal aortic aneurysm repair in Marfan syndrome. J Card Surg 1997;12:167-72.
2. Crawford ES, DeNatale RW. Thoracoabdominal aortic aneurysm: observations regarding the natural course of the disease. J Vasc Surg 1986;3:578-82.
3. Hasham SN, Guo DC, Milewicz DM. Genetic basis of thoracic aortic aneurysms and dissections. Opin Cardiol 2002;17:677-83.
4. Segura AM, Luna RE, Horiba K, Stetler-Stevenson WG, McAllister HA, Willerson JT, et al. Immunohistochemistry of matrix metalloproteinases and their inhibitors in thoracic aortic aneurysms and aortic valves of patients with Marfan's syndrome. Circulation 1998;98:II-331–8.
5. Rojo-Leyva F, Ratliff NB, Cosgrove DM 3rd, Hoffman GS. Study of 52 patients with idiopathic aortitis from a cohort of 1,204 surgical cases. Arthritis Rheum 2000;43:901-7.
6. Takagi H, Mori Y, Iwata H, Kimura M, Itokazu M, Shimokawa K, et al. Nondissecting aneurysm of the thoracic aorta with arteritis in systemic lupus erythematosus. J Vasc Surg 2002;35:801-4.
7. Khan AS, Spiera H. Association of aortic aneurysm in patients with systemic lupus erythematosus: a series of case reports and a review of the literature. J Rheumatol 1998;25:2019-21.
8. Faye-Petersen OM, Arnold MM, Grizzle WE, Lie JT. Lymphoplasmacytic aortitis and acute aortic dissection: an uncommon association. Arch Pathol Lab Med 1996;120:402-4.
9. Willett WF 3rd, Kahn MJ, Gerber MA. Lupus aortitis: a case report and review of the literature. J LA State Med Soc 1996;148:55-9.
10. Kumar V, Abbas AK, Fausto N, editors. Robbins & Cotran: pathologic basis of disease, 7th ed. Philadelphia: Saunders; 2005. p. 523-36.
11. Haug ES, Skomsvoll JF, Jacobsen G, Halvorsen TB, Saether OD, Myhre H. Inflammatory aortic aneurysm is associated with increased incidence of autoimmune disease. J Vasc Surg 2003;38:492-7.
12. Niianami H, Shigeyuki A, Tagusari O, Hashimoto A, Koyanagi H. Extensive aortic reconstruction in Marfan syndrome. Ann Thorac Surg 1999:67:1864-7.
13. Finkbohner R, Johnston D, Crawford S, Coselli j, Milewicz D: Aortas/pulmonary arteries: Marfan syndrome: long-term survival and complications after aortic aneurysm repair. Circulation 1995;91:728-33.

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